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MicroNAPS: A Novel Classification for Infants with Micrognathia, Robin Sequence, and Tongue-based Airway Obstruction

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Background: Robin sequence (RS) describes a heterogeneous population with micrognathia, glossoptosis, and upper airway obstruction (UAO). Workup, treatment, outcomes assessment, and research inclusion are widely variable. Despite several classifications and algorithms, none is broadly endorsed. The objective of this investigation was to develop and trial a novel classification system designed to enhance clinical communication, treatment planning, prognostication, and research.
Methods: This is a retrospective cross-sectional study. A classification system was developed with five elements: micrognathia, nutrition, airway, palate, syndrome/comorbidities (MicroNAPS). Definitions and a framework for "stage" assignment (R0–R4) were constructed. Stage "tongue-based airway obstruction" (TBAO) was defined for infants with glossoptosis and UAO without micrognathia. MicroNAPS was applied to 100 infants with at least 1-year follow-up. Clinical course, treatment, airway, and feeding characteristics were assessed. Descriptive and analytic statistics were calculated and a *P* value less than 0.05 was considered significant.
Results: Of the 100 infants, 53 were male. Mean follow-up was 5.0 ± 3.6 years. R1 demonstrated feeding-predominant mild RS for which UAO was managed nonoperatively but gastrostomy tubes were prevalent. R2 was characterized by airway-predominant moderate RS, typically managed with mandibular distraction or tongue-lip adhesion, with few gastrostomy tubes and short lengths-of-stay. R3 denoted severe RS, with similar UAO treatment to R2, but with more surgical feeding tubes and longer admissions. R4 represented a complex phenotype with 33% tracheostomies, protracted hospitalizations, and delayed palatoplasty. R0 ("at risk") and TBAO groups displayed the most variability.
Conclusions: MicroNAPS is easy to use and associated with relevant disease characteristics. We propose its adoption in clinical and research settings. *(Plast Reconstr Surg Glob Open 2023; 11:e5283; doi: 10.1097/GOX.0000000000005283; Published online 19 September 2023.)*

INTRODUCTION

Micrognathia has been linked to breathing and feeding dysfunction since the late 1800s.[1] The eponym for the triad of mandibular hypoplasia (micrognathia), retropositioning of the tongue (glossoptosis), and upper airway obstruction (UAO) honors Pierre Robin, the French stomatologist who publicized the associations in 1923.[2] Initially described as an "anomalad"[3] or syndrome,[4] this clinical picture is now recognized as a sequence of anomalies initiated by micrognathia[5,6] and with myriad etiologies. A cleft of the secondary palate, distinct from the more common cleft lip and palate,[7] is often present and likely originates from mechanical obstruction of palatal fusion by the unfavorable tongue position.[8]

Robin sequence (RS) literature suffers from heterogeneity as diverse as the diagnosis,[9] rendering most studies incomparable. Inconsistency ranges from the components of the diagnosis (can a child with an intact palate have RS?[10]), to the diagnostic workup (should polysomnography

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be standard?[11]), to treatment (surgical treatment abounds in the United States but is rare in Europe[12]), to labeling (Robin sequence versus Pierre Robin sequence[13]). Over three international consensus conferences, the former and latter debates have been settled: RS can exist in the absence of clefting[14] and, pursuant to traditional eponymous naming practices, only the family name is used: Robin sequence.[13] Less progress has been made toward standardizing workup and management. Several algorithms and classifications have been proposed,[11,15–26] but none is broadly embraced.

One factor handicapping communication, prognostication, and research is lack of a universal classification system. At the extremes, a child with RS, Treacher Collins syndrome, and severe UAO requiring tracheostomy is not comparable to one with nonsyndromic RS, minor UAO, and proficient oral feeding. Further, "syndromic" versus "nonsyndromic," as often aggregated in research, is an insufficient discriminator considering the more than 40 associated syndromes with substantially diverse implications.[27,28]

The purpose of this investigation was to develop and test a novel classification system for infants with micrognathia, RS, and/or tongue-based airway obstruction (TBAO). The proposed classification leverages factors obtained from examination and tests with pertinent implications to treatment and prognosis. A primary classification scheme and variations are presented to promote broad adoption, independent of resources and preferences. The framework is designed to be modifiable as knowledge evolves. This classification is not intended to dictate management but rather to improve communication and support rigorous research stratification.

Takeaways

Question: Infants with Robin sequence (RS) have disruption in breathing and feeding in infancy. The diagnosis is extremely heterogeneous, and no universal treatment pathway exists. A clinically applicable classification system is necessary to guide management decisions.

Findings: We created a novel classification with five elements and a summary stage (R0–R4) using the acronym MicroNAPS. We tested this classification in a sample of 100 infants with RS and found it to be easily applicable and correlated to important variables, including surgical decisions and feeding outcomes.

Meaning: MicroNAPS classification should be adopted to augment clinical communication, support treatment decisions, predict outcomes, and stratify research in RS care.

MATERIALS AND METHODS

Study Design

This is a retrospective cross-sectional study, including infants with micrognathia, RS, and/or TBAO. One hundred infants with at least 1-year follow-up were selected from a departmental micrognathia database, which includes nearly 400 patients, from 2005 to 2021. Sequential patients were queried from earliest date forward until 100 subjects meeting criteria were identified. Demographics, birth history, clinical findings, polysomnograms (PSG), feeding characteristics, and syndromes/comorbidities were recorded. The primary predictor variable was MicroNAPS stage. Outcome variables included clinical course, treatment, and airway and feeding characteristics. This project was approved by the institutional review board (protocol #P00023123).

MicroNAPS

This classification system includes five elements, illustrated by the acronym MicroNAPS (Tables 1 and 2). Staging is assigned according to Table 3. Documentation models the TNM system of tumor staging[29]: elements are recorded with subscript scores followed by corresponding stage (Figs. 1 and 2). Alternate airway criteria that may be substituted for primary PSG measures are described in Table 4. To facilitate application at initial evaluation, often before complete data availability, modifiers may be

Table 1. MicroNAPS Classification of Infants with Micrognathia, RS, and/or Tongue-based Airway Obstruction

Element	0 (Normal)	1 (Minor)	2 (Moderate)	3 (Severe)
Micrognathia	Normal (overjet <3 mm)	Mild (overjet 3 to <6 mm)	Moderate (overjet 6 to <10 mm)	Severe (overjet ≥10 mm)
Nutrition	Full PO, meeting caloric and weight goals	Full PO, not fully meeting caloric and/or weight goals	Feeds partially PO and partially enteric	Full enteric feeds
Airway	oAHI <5/h *AND* SpO_2 nadir >85%	oAHI 5–10/h *OR* SpO_2 nadir <85%	oAHI 11–20/h	oAHI >20/h *OR* $P_{ET}CO_2$ > 50 torr for >50% TST *OR* Tracheostomy *OR* Intubated (may be downgraded after extubation)
Palate	Intact/submucous	Veau I cleft	Veau II cleft	Veau ≥ III cleft
Syndrome/comorbidities	No impactful syndrome or comorbidities	MINOR impact to neonatal management	MODERATE impact to neonatal management	SEVERE impact to neonatal management

PO, per os; oAHI, obstructive apnea-hypopnea index; SpO_2, oxygen saturation; $PETCO_2$, end-tidal carbon dioxide; TST, total sleep time.

Table 2. Scoring of Syndromes and Comorbidities

1 (Minor)		2 (Moderate)		3 (Severe)	
Syndrome/Comorbidity, n Sample		**Syndrome/Comorbidity, n Sample**		**Syndrome/Comorbidity, n Sample**	
Birth <38 but ≥34 weeks GA	0	Birth at <34 but ≥29 weeks GA	0	Birth at 28 weeks GA or earlier	0
Gastroesophageal reflux disease (GERD)	18	Hypotonia	7	Congenital cardiac anomaly (complex—ie, Tetralogy of Fallot)	13
Congenital cardiac anomaly (minor—ie, ASD)	10	Hemifacial/craniofacial microsomia	6	Nager syndrome	3
Stickler syndrome	7	Laryngomalacia (severe)	4	Cerebellar hemorrhage	1
Laryngomalacia (minor)	6	Trisomy 18	2	Hypoxic encephalopathy	1
Global developmental delay/ intellectual disability	5	Auriculocondylar syndrome	1	Kabuki syndrome	1
Choanal atresia/stenosis	3	Bardet-Biedl syndrome	1	Muscular dystrophy	1
Club feet	2	Bronchomalacia	1	Treacher Collins syndrome	1
Hearing loss	1	Bronchopulmonary dysplasia	1		
Insulin dependent diabetes mellitus	1	Catel Manzke syndrome	1		
Multi-cystic kidney disease	1	Cornelia de Lange syndrome	1		
Omphalocele	1	Diabetes insipidus	1		
Skeletal dysplasia	1	Diaphragmatic hernia	1		
Torticollis	1	EBPF3 disorder (HADD syndrome)	1		
Ventriculomegaly	1	Laryngeal cleft	1		
Vocal fold paralysis	1	Microcephaly	1		
		Neonatal abstinence syndrome	1		
		Oculocutaneous albinism	1		
		Prader Willi syndrome	1		
		Restrictive lung disease	1		
		SHORT syndrome (PIK3R1 mutation)	1		
		Shprintzen-Goldberg syndrome	1		
		Soto syndrome	1		
		Townes-Brocks syndrome	1		
		Trisomy 21	1		
		22q11.2 syndrome	0		

Number of subjects with each diagnosis included in the sample population appear to the right of each diagnosis.

Table 3. Staging of RS, TBAO, and "at Risk" for RS (R0) Based on MicroNAPS Elements

Stage	Micro	N	A	P	S
TBAO	0	1–3	1–3	Any	Any
R0	1—3	Any	0	Any	0–1
R1	1–3	1	1	Any	0–2
R2	1–3	2	2	Any	0–2
R3	1–3	3	3	Any	0–2
R4	1–3	1–3	1–3	Any	3

Stage is assigned based on the highest score in any element column.
Micro, micrognathia; N, nutrition; A, airway; P, palate; S, syndrome/comorbidities.

applied according to Table 5. Scoring examples are provided in Table 6.

Analysis

Descriptive statistics are presented as absolute values (n_{100} = n%). Univariate logistic or linear regressions were applied as applicable to assess the effect of MicroNAPS stage. Chi-square with Bonferroni post hoc tests were calculated for ordinal bivariate comparisons. Statistical significance was set as a *P* value less than 0.05.

RESULTS

Sample

Of the 100 infants, 53 were male, and 70 were non-White. Mean gestational age at birth was 37 weeks 4.9 days ± 2.8 weeks, and birthweight was 2904 ± 732.3 g. Syndromes/comorbidities are shown in Table 2. Hospital length of stay (LOS) was 52.5 ± 31.5 days (range 4–134 days), and follow-up was 5.0 ± 3.6 years (range 1–15.7 years). MicroNAPS scores are presented in Figures 3 and 4.

Nonoperative treatment for UAO was trialed for all, but used as definitive management for only 32 infants, including positioning; supplemental oxygen and/or nasopharyngeal airway, n = 23; continuous positive airway pressure, n = 7; and orthodontic airway plate, n = 2. Operations for UAO were performed in 68 infants at mean age 9.8 ± 14.8 weeks-of-life, including: tongue-lip adhesion (TLA), n = 9; mandibular distraction (MDO), n = 52; tracheostomy, n = 7. Latest follow-up PSG data at age 1.5 ± 2.4 years (n = 90) demonstrated mean obstructive apnea-hypopnea index 4.6 ± 10.8/hour and did not differ by treatment ($P = 0.116$).

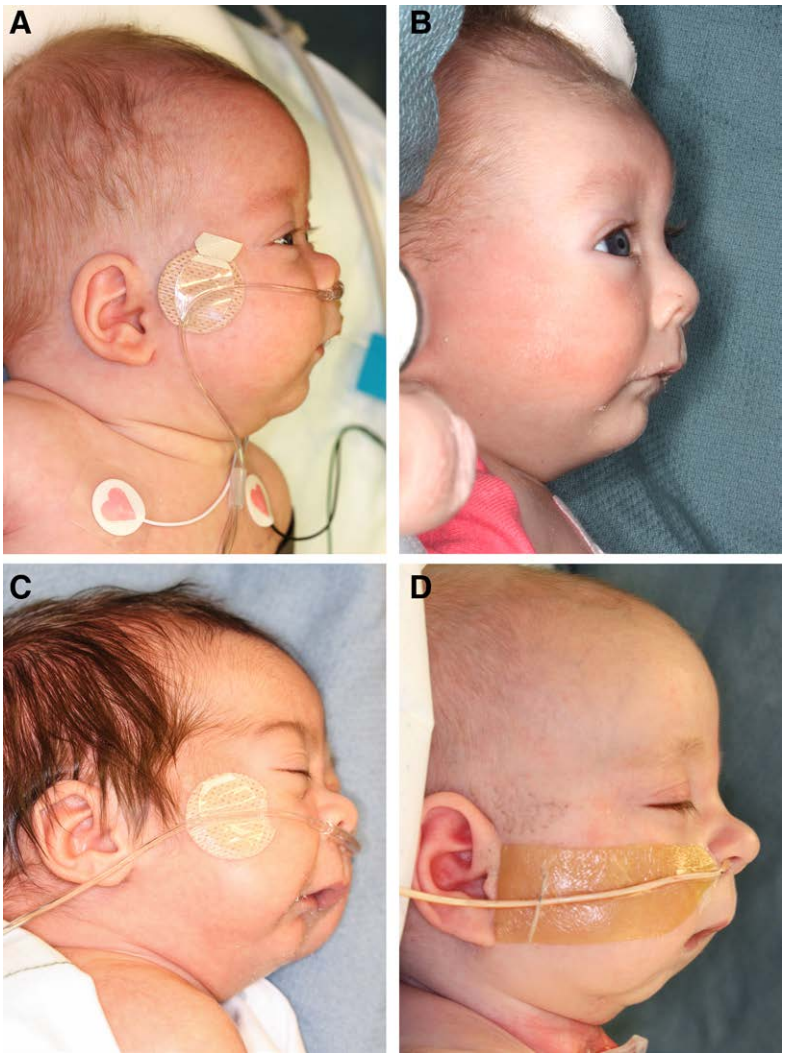

Fig. 1. Examples of micrognathia scoring by clinical examination. A, normal ($Micro_0$); B, minor ($Micro_1$); C, moderate ($Micro_2$); and D, severe ($Micro_3$).

Associations

Treatment for UAO

Stages R0–R1 were predominantly treated nonoperatively (95%), whereas stages ≥R2 most frequently had an operation (86%, $P < 0.001$). R0 was the only group with failures of the initial nonoperative treatment strategy (23%), subsequently necessitating an operation. TLA or MDO comprised nearly all operations for R2 and R3 (n = 1 tracheostomy, R3), but, for R4, 38% of operations were tracheostomies ($P < 0.001$; Table 7).

Gastrostomy Tubes

The rate of gastrostomy tube (G-tube) insertion was highest for R1. Importantly, our surgical pathways for TLA and tracheostomy (but not MDO) include placement of a G-tube. Therefore, while overall G-tube rates were similar between R2 and R3, when "G-tubes by pathway" were excluded, the rate was significantly higher for R3 (22% versus 8%, $P < 0.001$).

Length of Stay

LOS was most variable for R0 (range 9-133 days) and TBAO (range 4–112 days). LOS was shortest for R2 (32 ± 14.5 days), longer for R3 (54.6 ± 28.4 days), and longest for R4 (62 ± 28.1 days).

Palatoplasty Timing

Palatoplasty was most delayed for R0 (14.2 ± 8.9 months) ($P < 0.04$) and trended later for R4 (13.0 ± 4.9 months) and TBAO (n = 1, 12 months) ($P > 0.353$). Palatoplasties occurred within our typical timeline (9–11 months) for R1–R3.

DISCUSSION

The triad of micrognathia, glossoptosis, and UAO termed RS describes a phenotype with myriad etiologies and impacts. Existing classifications fall short in correlation to management and prognosis. A scheme to stratify patients with this heterogeneous diagnosis is critical to facilitate communication, prognostication, and research.

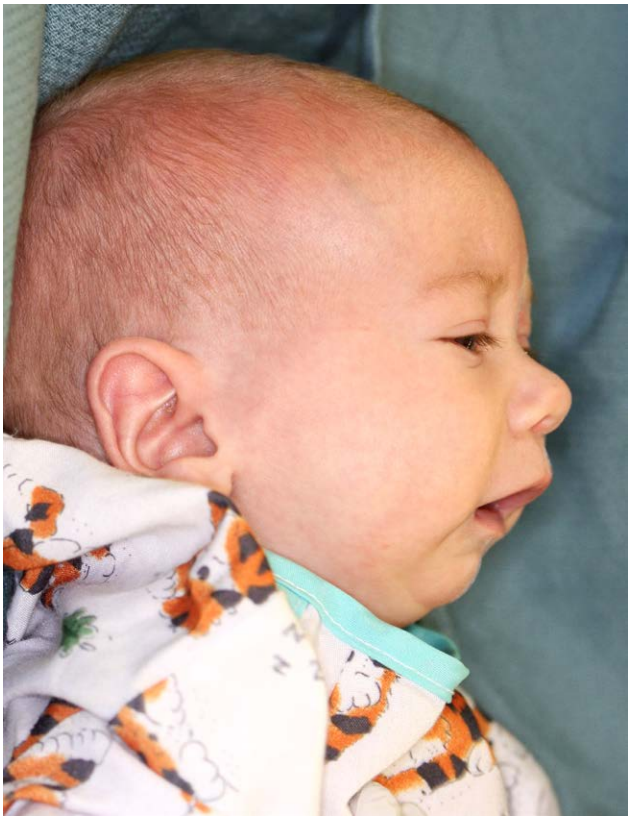

Fig. 2. Infant with Micro$_2$N$_2$A$_3$P$_2$S$_1$, Stage R3. She displays moderate micrognathia, is meeting caloric and weight targets by partial PO feeding supplemented with gavage feeds by nasogastric tube, had a PSG with oAHI of 16/hour, SpO_2 nadir of 82%, and 55% of total sleep time with $P_{ET}CO_2$ of more than 50 torr, has a Veau II cleft palate, and received a prenatal diagnosis of a COL2A1 gene mutation (Stickler syndrome type I). Note that the $P_{ET}CO_2$ pushed the airway score to 3 (severe) despite oAHI in the moderate range. The A_3 element score subsequently drove the stage designation of R3 in this example.

Rationale for MicroNAPS

For a novel system to be adopted, it must be relevant, simple, memorable, and sufficiently broad for universal application but appropriately specific to achieve prognostic impact. The TNM oncology staging system is an example of a design with these attributes.[29] Within craniofacial surgery, one of the most ubiquitous classifications is the OMENS score for hemifacial microsomia.[33] Despite conception in the era of two-dimensional imaging, OMENS scores are still proclaimed in halls of craniofacial clinics worldwide. MicroNAPS builds on the attributes of the TNM and OMENS structures.

MicroNAPS represents an amalgamation of prior systems, existing literature, and clinical experience. The earliest RS classification, proposed by Couly et al[15] in 1988 and revised by Caouette-Laberge and colleagues[16] in 1994, included three groups: (1) adequate respiration when prone, bottle feeding; (2) adequate respiration when prone, gavage feeding; (3) respiratory distress requiring intubation and gavage feeding. The 2008 West Midlands grading[18] added subjective assessment of glossoptosis. Rogers et al correlated additive GILLS scores (gastroesophageal reflux, intubation, late operation, low birth weight, syndromic) with TLA outcomes in 2011.[19,20,25,34] Separate UAO and feeding domains were introduced by the Montreal Classification[21] in 2015. The Vancouver Classification[22] of 2017 contributed a hierarchical structure with emphasis on degree of micrognathia, glossoptosis, oximetry, and prior failed treatment. Each system has augmented RS care, but none has been universally adopted. Shortcomings include oversimplicity, narrow application, exceeding subjectivity, and/or reliance on treatment outcomes for stratification. Attributes of each have informed MicroNAPS.

The five element scores of MicroNAPS facilitate succinct and relevant clinical communication, and the stage summarizes characteristics for treatment planning, prognostication, and research design. MicroNAPS elements

Table 4. Alternate Criteria for the Airway Element in MicroNAPS

Alternate Airway Criteria	0 (Normal)	1 (Minor)	2 (Moderate)	3 (Severe)
Mixed obstructive apnea-hypopnea index (MOAHI) from PSG Adopted from Lim et al 2022[30]	MOAHI < 1	MOAHI 1–5	MOAHI 5–10	MOAHI > 10
Awake flexible fiberoptic laryngoscopy (FFL) Adapted from Yellon et al 2006[31]	Normal	Epiglottic prolapse against the posterior pharyngeal wall with airway obstruction but normal tongue position	Prolapse of the epiglottis and tongue base with only the epiglottic tip epiglottis visible and obliteration of the vallecula	Complete collapse of tongue against the posterior pharyngeal wall and no portion of epiglottis visible
Drug-induced sleep endoscopy (DISE) Adapted from Chan et al 2014[32]	No obstruction (complete view of vallecula)	0%–50% obstruction (vallecula not visible)	50%–99% obstruction (epiglottis not contacting posterior pharyngeal wall)	Complete obstruction (epiglottis against posterior pharyngeal wall)
Clinical examination and pulse oximetry Adapted from Cole et al 2008[18]	–No desaturations on pulse oximetry –No respiratory distress when nursed supine –Inconsistent glossoptosis	–Desaturations with feeding, but able to complete feeds –Consistent but mild respiratory distress when supine –Consistent glossoptosis –Maintaining milestones with assistance (ie, modified feeding techniques)	–Desaturates routinely when supine –Unable to maintain adequate nutrition intake without intervention (nasogastric or gastrostomy tube)	–Desaturates routinely when prone –May require intubation

Table 5. MicroNAPS Modifiers

Modifier	Element	Definition
A	Airway	Alternate airway criteria applied
NA	Airway	Airway not assessed (update expected as data become available)
IN	Airway	Intubated
T	Airway	Tracheostomy present
GI	Nutrition	Primary gastrointestinal explanation for feeding dysfunction

include: micrognathia, nutrition, airway, palate, and syndrome/comorbidities.

Micrognathia

Micrognathia is understood to be the initiating feature of RS and the cause of the glossoptosis, UAO, feeding dysfunction, and clefted palate that may follow.[11,35] Many authors have described methods to quantify micrognathia,[17,22,36–39] but no accepted definition exists. Further, correlation between degree of micrognathia and severity of UAO and feeding dysfunction is variable.[40] Some infants without micrognathia manifest findings similar to RS (TBAO).[41] The degree of micrognathia is relevant in the conceptual framework of RS and for communication amongst providers but has minimal influence on initial management. As such, the micrognathia score is qualitative rather than quantified, and is not weighted in staging.

Nutrition

Feeding dysfunction is a hallmark of RS and loosely tracks with UAO.[42] Up to 70% of infants with RS require enteral feeding.[43] The etiology of feeding and growth restriction in RS is multifactorial. Airway obstruction contributes to feeding impairment by disruption of the suck-swallow-breath reflex.[14] Even with adequate supplementation, however, infants with RS frequently demonstrate restricted growth, likely due to metabolic expenditure from obstructed breathing.[44] Up to 50% of infants with RS receiving enteral feeds continue to be malnourished.[45] After UAO is resolved, infants enter a period of "catch up," with growth rates surpassing those of age-matched children.[46] Growth is covariate to feeding, and feeding is highly influenced by UAO; the web of feeding-growth-airway interactions outmatches any classification scheme. As the ability to achieve daily caloric intake partially or completely via PO feeding represents a surrogate marker for feeding capability, this is the target of the nutrition element in MicroNAPS.

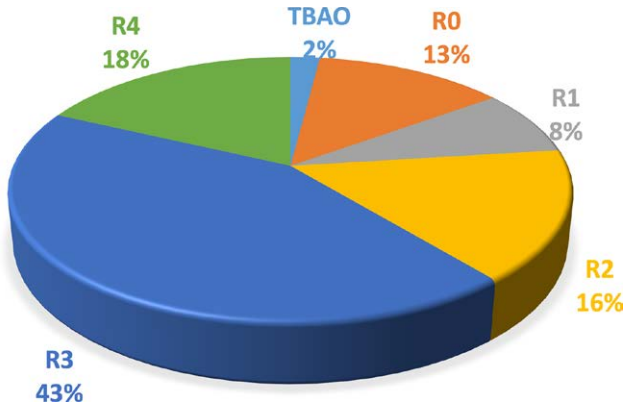

Fig. 3. MicroNAPS stages in the study sample.

Airway

UAO is the core finding that drives treatment and prognosis in infants with RS. Clinical observation and oxygen saturation monitoring underestimate the frequency and severity of obstruction.[21] Indeed, only 54% of micrognathic infants with obstructive sleep apnea (OSA) snore.[47] When respiratory distress is observed, PSG has demonstrated severe OSA in 74%.[42] PSG has therefore become the gold standard diagnostic test for OSA.

The most used PSG-based definition for OSA in children is apnea-hypopnea index (AHI) of more than 1 per hour.[48] This cutoff, however, neglects unique characteristics of infant breathing. Older children rarely experience airway obstruction; so AHI of more than 1 per hour reasonably captures sleep disordered breathing in that cohort. On the contrary, normative infant data demonstrate frequent baseline obstruction. Obstructive AHIs from 2.3 to 4.9 per hour have been reported in healthy infants.[49,50] Thus, AHI of more than 1 is an overly broad definition for OSA in infants.

Unlike in older patients, infant airway obstruction is not confined to sleep; UAO in infants occurs during REM and non-REM sleep and during wakefulness. To recognize independence from sleep cycles, the term "upper airway obstruction" is preferred over "obstructive *sleep* apnea" in infants. Further, some central apnea is physiologically normal in infants.[51] We applied current knowledge of pediatric sleep physiology and propose new definitions for UAO

Table 6. Examples of Use of MicroNAPS and Modifiers, Beginning with the Infant Shown in Figure 2 (Micro2N2A3P2S1, Stage R3)

Modification from the Infant in Figure 2	Element Scores	Stage
Airway evaluation by DISE (without PSG), with complete oropharyngeal obstruction and epiglottis abutting pharyngeal wall	$Micro_2N_2A_{3A}P_2S_1$	R3A
Initial classification while PSG results are pending	$Micro_2N_2A_{NA}P_2S_1$	R2NA
Tracheostomy present	$Micro_2N_2A_{3T}P_2S_1$	R3T
Intubated (may be downgraded after extubation and airway assessment)	$Micro_2N_2A_{3IN}P_2S_1$	R3IN
Gastrostomy tube for primary gastrointestinal indication	$Micro_2N_{GI}A_3P_2S_1$	R3GI
Normal mandibular position (no micrognathia)	$Micro_0N_2A_3P_2S_1$	TBAO
PSG with oAHI 3/h, SpO_2 nadir 94%	$Micro_2N_2A_0P_2S_1$	R0

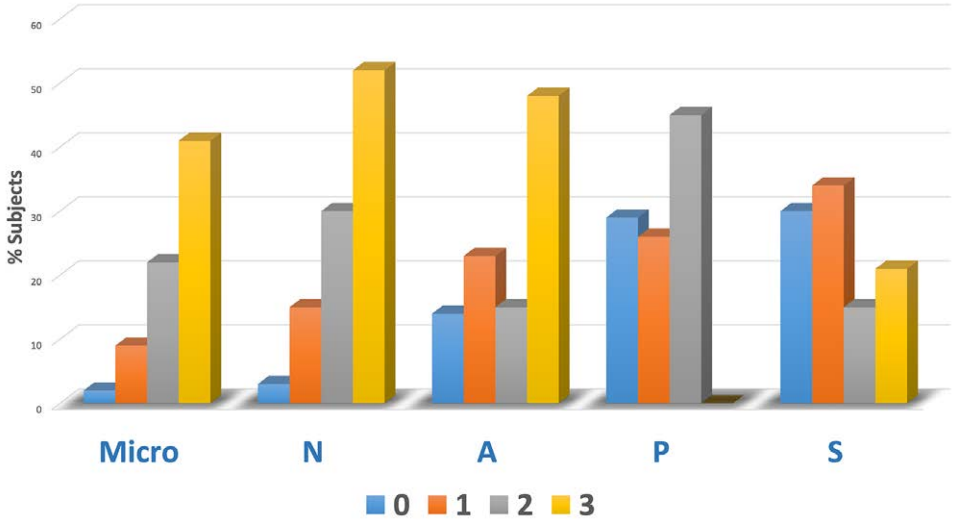

Fig. 4. MicroNAPS element scores in the study sample.

Table 7. Study Outcomes by MicroNAPS Stage

Outcome	R0	R1	R2	R3	R4	TBAO	
n	13	8	16	43	18	2	***P***
Primary treatment type							**<0.001**
Positioning, O_2, ±NP	11 (84%)	7 (88%)	2 (13%)	1 (2%)	0	1 (50%)	
CPAP	1 (8%)	0	1 (6%)	1 (2%)	2 (11%)	0	
OAP	0	1 (12%)	0	1 (2%)	0	0	
TLA	0	0	4 (25%)	6 (14%)	0	0	
MDO	1 (8%)	0	9 (56%)	33 (78%)	10 (56%)	1 (50%)	
Tracheostomy	0	0	0	1 (2%)	6 (33%)	0	
Primary Tx by operation	1 (8%)	0	13 (81%)	40 (93%)	16 (89%)	1 (50%)	**<0.001**
Primary Tx strategy failed	3 (23%)	0	0	0	0	0	**<0.001**
oAHI from f/u PSG (events/h)	1 ± 1.9	3.6 ± 5.2	2.6 ± 4.8	5.5 ± 11.9	7.7 ± 16.7	3.1 ± 2	0.562
Full PO 30 d after discharge	2 (17%)	3 (38%)	7 (44%)	25 (61%)	8 (44%)	1 (50%)	0.341
NG tube at discharge	5 (42%)	0	4 (25%)	2 (5%)	1 (6%)	1 (50%)	
Gastrostomy tube total	5 (42%)	5 (63%)	5 (31%)	14 (34%)	9 (50%)	0	
Gastrostomy tube not by pathway*	5 (42%)	5 (63%)	1 (8%)	8 (22%)	3 (17%)	0	0.286
Length-of-stay in hospital	60.6 ± 58.4	50.5 ± 27.5	32 ± 14.5	54.6 ± 28.4	62 ± 28.1	58 ± 76.4	0.176
Months at palatoplasty (n = 57)	14.2 ± 8.9	9.8 ± 1.5	9.7 ± 0.9	10.1 ± 0.9	13 ± 4.9	12	**0.014**

Values in boldface indicate statistical significance.
*Pathway indicates insertion of a gastrostomy tube by surgical pathway rather than because of by feeding dysfunction.
O_2, supplemental oxygen; NP, nasopharyngeal airway; CPAP, continuous positive airway pressure; OAP, orthodontic airway plate; TLA, tongue-lip adhesion; MDO, mandibular distraction osteogenesis; Tx-treatment; oAHI, obstructive apnea-hypopnea index; NG, nasogastric tube.

for infants, with adjusted oAHI cutoffs and recognition of the relevance of hypoxemia and hypercapnia.

PSG is an expensive test[30] with variable interpretation,[52] and is not available for infants in many centers.[31,53,54] Although we strongly advocate for inclusion of PSG in standard evaluation of infants with suspected RS, alternate definitions for UAO are necessary for MicroNAPS to be applied when PSG remains unavailable. When alternative airway criteria have been used, the "A" modifier is applied to the stage designation to denote deviation from more thoroughly vetted definitions of UAO.

Diagnostic tests that may be substituted for PSG when necessary (Table 4) include endoscopic airway examinations [awake flexible fiberoptic laryngoscopy (FFL), drug-induced sleep endoscopy (DISE)], and the combination of clinical examination and pulse oximetry.[18] FFL is routinely performed for visualization of the site(s) of upper airway collapse.[11,17] Inclusion of FFL in primary airway classification, however, is hindered by its subjective nature, lack of standardized grading,[55,56] and variability induced by positioning and other factors.[57] The predictive value for diagnosing TBAO by awake FFL is variable[32]; Lee et al demonstrated a false negative rate of 50%.[58]

DISE observes upper airway dynamics in conditions that mimic natural sleep. DISE decreases inter-observer variability compared with FFL,[59] but no scoring system is universally implemented. In VOTE, the most widely used classification,[60] each region specified in the acronym (Velum, Oropharyngeal lateral walls, Tongue base, Epiglottis) is classified by configuration (anterior-posterior,

lateral, or concentric), and degree (no, partial, or complete) of obstruction. VOTE, however, was described in adults and is not directly applicable to infants. Chan and colleagues proposed a DISE stratification for children in 2014[61] using a four-point ordinal scale (0–3) to grade degree of obstruction at each of five levels (adenoids, velum, lateral pharyngeal wall, tongue base, and supraglottis). This system was further validated in 23 patients with mean age 2.2 years and remains the only substantiated DISE grading scheme for children.[62]

Airway analysis continues to evolve as technology and research improve. Emerging techniques such as four-dimensional computed tomography and computational fluid dynamics[63] may ultimately augment or supplant PSG. MicroNAPS and the proposed Alternate Airway Criteria are designed to provide a framework to support adaptation of future knowledge in subsequent versions.

Palate

A cleft palate is seen in 70%–90% of children with RS and likely results from mechanical obstruction of palatal fusion by the ectopically positioned tongue during fetal development.[8,16] Clefting alters feeding technique and augments operative needs by necessitating palatoplasty, myringotomy tubes, and/or speech surgery. Palatoplasty may transiently worsen UAO.[64] Infants with isolated palatal clefts without RS, however, are spared the amplified caloric need and growth restriction characteristic of the RS phenotype.[65] Palatal clefting is included as an element of MicroNAPS to facilitate disclosure of salient patient characteristics, but, commensurate to its minor effect on early management, this element is not weighted in staging.

Syndrome/Comorbidities

The etiopathogenesis of the RS phenotype is exceptionally diverse. Primary mandibular hypoplasia, growth inhibition induced by oropharyngeal muscle hypotonia, and in utero mandibular compression have all been postulated as the pathogenesis.[66] More than 40 genetic syndromes and myriad comorbidities are associated with RS.[27] Comorbid anomalies are present in up to 70%, many without recognized genetic origin.[67] RS research often partitions subjects into "nonsyndromic" and "syndromic" buckets, sometimes adding "(P)RS-plus" to indicate comorbid conditions not known to be genetically based.[68] Advances in genetic research suggest that even children considered "nonsyndromic" may have a genetic basis for the RS phenotype.[69]

Implications of the genotype on early management and prognosis are as diverse as the multitudinous diagnoses. Some diagnoses impact early management and prognosis of UAO and feeding; others have little effect on airway and nutrition despite implications to other facets of well-being. Stickler syndrome, for example, has a favorable expectation for facial growth and resolution of UAO. Conversely, children with Treacher Collins syndrome have poor craniofacial growth and frequently require aggressive and/or repeated interventions to resolve UAO.[28]

For this classification, the *impact to early RS management* is weighted more heavily than other repercussions of the diagnosis. To assess *impact to early RS management*, consider the following: Does the diagnosis imply diminished… (1) respiratory drive? (eg, neurologic disease); (2) respiratory efficiency? (eg, hypotonia, extreme prematurity); (3) cardiopulmonary reserve? (eg, congenital cardiac disease); (4) craniofacial growth capacity? (eg, Treacher Collins, Nager syndromes); (5) response to interventions for UAO? (eg, laryngomalacia). Examples of suggested scoring for syndromes and comorbidities are provided (Table 2) but are not exhaustive; clinical judgement must be applied.

Glossoptosis is notably absent from MicroNAPS despite its role in the mechanistic sequence from micrognathia to UAO. As UAO is covariate, the consequence of glossoptosis is captured in the airway score.[14] Further, grading of glossoptosis is highly subjective.[40] Direct assessment of glossoptosis, however, may prove paramount to identify the RS phenotype when other clinical factors cannot be evaluated, such as in prenatal diagnosis.[70]

Performance of MicroNAPS

Application of MicroNAPS to the sample population revealed relevant differences between stages. Summation of these findings enabled stage characterization as follows (Table 8).

R0 corresponds to an "at risk" group, as UAO, which is a required feature for the RS diagnosis, is not present. As expected, infants in this group were primarily treated nonoperatively. However, 23% went on to develop UAO, failed nonoperative management, and proceeded to surgery within their first year of life. Hospital length of stay was highly variable, ranging up to 133 days, and palatoplasty was often delayed. In summary, R0 includes significant diversity; close follow-up and high index of suspicion for development of UAO are required.

R1 represents "mild RS." All UAO was successfully treated nonoperatively. Interestingly, this group had the highest rate of G-tube insertion (63%). We conclude that R1 demonstrates a feeding-predominant RS phenotype.

R2 signifies "moderate RS." Most patients were managed with MDO or TLA; none received a tracheostomy. Temporary (nasogastric) feeding tubes were favored over surgical ones, length of stay was shortest, and palatoplasty was not delayed. R2 demonstrates an airway-predominant RS that responds predictably and expeditiously to surgical treatment. We plan to investigate the utility of orthodontic airway/pre-epiglottic baton plates in lieu of surgery for this group.

R3 denotes "severe RS." Like in R2, most UAO was successfully resolved with MDO or TLA. Compared with R2, however, comorbidities were more complex, G-tubes were more frequent, and hospitalizations were longer. R2 and R3 capture the most typical children for whom a craniofacial surgeon would be consulted early. We propose that future research regarding surgical management of RS enroll R2 and R3 rather than stratifying by "isolated and syndromic."

R4 describes a "complex" RS phenotype: 33% received tracheostomies, length of stay was prolonged, and palatoplasty was frequently delayed. The TBAO stage, although too sparse for analysis, demonstrated variability in treatment, hospital course, and palatoplasty timing. The heterogeneity of these two stages highlights the myriad

Table 8. Characterization of MicroNAPS Stages

Stage	Summary	Notable Findings
R0	At risk	• Primary treatment nonoperative (92%) • Only group with treatment failures requiring operation (23%) • Highly variable length of stay (range 9–133 d) • Palatoplasty frequently delayed (mean 14.2 ± 8.9 mo)
R1	Mild RS-feeding predominant	• All successfully treated nonoperatively • Highest rate of G-tubes (63%) • Normal palatoplasty timing
R2	Moderate RS-airway predominant	• Primary treatment by operation (MDO or TLA) (81%) • Lowest rate of G-tubes (8% not for pathway) • Shortest length-of-stay (32 ± 14.5 d) • Normal palatoplasty timing
R3	Severe RS	• Primary treatment by operation (MDO or TLA; Trach, n = 1) (93%) • Higher rate of G-tubes than R2 (22% not for pathway) • Longer length-of-stay than R2 (54.6 ± 28.4) • Normal palatoplasty timing
R4	Complex RS	• Primary treatment by operation (89%) • Highest rate of tracheostomy (38% of operations) • Longest length-of-stay (62 ± 28.1) • Palatoplasty frequently delayed (mean 13 ± 4.9 mo)
TBAO	Variable	• Variable treatment • Highly variable length-of-stay (range 4–112 d) • Palatoplasty may be delayed (mean 12 mo)

comorbidities contained within and necessity to anticipate management challenges.

Limitations

MicroNAPS is not without limitations. One drawback is reliance on PSG for airway scoring. Understanding of infant sleep physiology is evolving, and access to PSG is not universal. Alternate airway criteria are derived from existing literature but have not been directly compared with primary criteria. We see MicroNAPS as a framework to evolve with future scientific discovery. Another limitation is oversimplification of the nutrition element, which may not fully capture the intricate mosaic of feeding, metabolism, and growth, and which is subject to institutional preference regarding enteral nutrition strategy. Further, the syndrome/comorbidities element demands clinical judgement, introducing inter-rater variability. We postulate that simple characterization of these complex variables is most sustainable in a clinically based classification scheme. Finally, MicroNAPS is not validated beyond our sample, which may be biased by institutional norms and our designation as a quaternary-care children's hospital. More study is imperative to validate this system.

CONCLUSIONS

We present a novel classification for infants with micrognathia, RS, and/or TBAO. This classification is not intended to dictate treatment, but rather to provide a framework for consistent decision-making. We hope that MicroNAPS will clarify communication; forecast pragmatic workup, treatment, and prognosis; and define inclusion for research.

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DISCLOSURE

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PATIENT CONSENT

Parents or guardians provided written consent for the use of the patients' image.

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